General

Guideline Title

Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis.

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Apr. 55 p. (Technology appraisal guidance; no. 254).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Fingolimod is recommended as an option for the treatment of highly active relapsing–remitting multiple sclerosis in adults, only if:

- They have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon, and
- The manufacturer provides fingolimod with the discount agreed as part of the patient access scheme.

People currently receiving fingolimod whose disease does not meet the criteria described above should be able to continue treatment until they and their clinician consider it appropriate to stop.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Highly active relapsing-remitting multiple sclerosis (RRMS)

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Neurology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate the clinical effectiveness and cost-effectiveness of fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis

Target Population

Patients with highly active relapsing-remitting multiple sclerosis, who have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon

Interventions and Practices Considered

Fingolimod

Major Outcomes Considered

- Clinical effectiveness
  - Annualised relapse rate (ARR)
  - Confirmed disability progression at 3 month
  - Mortality
  - Adverse reactions to treatment
  - Health related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Evidence Review Group (ERG) report for this appraisal was prepared by the Centre for Review and Dissemination (CRD) and Centre for Health Economics (CHE) Technology Assessment Group (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description of Manufacturer's Search Strategy and Comment on Whether the Search Strategy Was Appropriate

The manufacturer's submission described the search strategies used to identify relevant studies of fingolimod for the treatment of relapsing-remitting multiple sclerosis (RRMS). Comparators searched for were: beta interferon, glatiramer acetate, natalizumab, and standard care.

Search Strategy for Clinical Evidence

The manufacturer's submission gave detailed descriptions of the search strategies and met NICE requirements. It included the specific databases searched (MEDLINE, MEDLINE In-Process, EMBASE and The Cochrane Library) and the service providers used, the date span of searches and the date searches were run. It also included the complete strategies used and the results for each set. The following Web sites were searched for conference abstracts that were published from 2008 to April 2010: American Academy of Neurology, Americas Committee for Treatment and Research in Multiple Sclerosis, European Committee for Treatment and Research in Multiple Sclerosis, European Charcot Foundation. Reference lists of the included studies and reviews were also searched for relevant studies.

There were some inappropriate elements in the search strategies used, such as the use of a facet to search the Cochrane Library for randomised controlled trials (RCTs) and use of economic studies search terms for National Health Service Economic Evaluation Database (NHS EED) (these are inappropriate due to the content of the respective databases), and relevant material may have been missed as a consequence. However, the ERG did not identify any relevant studies which were not identified by the manufacturer's search. The search for clinical evidence may therefore be considered fit for purpose despite its non-ideal construction. As the searches for adverse events data, the mixed treatment comparison (MTC) and non-RCT evidence employed the same strategy, they may also be considered fit for purpose, with the additional caveat that the use of a filter for both RCTs and non-RCTs (detailed in the manufacturer's submission) may have contributed to relevant material being missed.

Statement of the Inclusion/Exclusion Criteria Used in the Study Selection and Comment on Whether They Were Appropriate

The inclusion criteria used in the systematic review process were studies of patients with RRMS treated with the following interventions: fingolimod, any beta-interferon at all doses, glatiramer acetate, natalizumab, and best supportive care (BSC). Mitoxantrone was excluded from the review. Trials of cladribine were included in the initial stage of study identification but subsequently excluded. RCTs, non-RCTs, long-term follow up studies and prospective observational studies, which were defined as phase IV studies were included. Relevant outcomes were relapse rate (mean annualised relapse rate [ARR] and patients remaining relapse free), disability progression (expanded disability status scale [EDSS] score and confirmed disability progression), disease activity, mortality, magnetic resonance imaging (MRI) measures, safety and tolerability (including adverse event data and withdrawals from treatment) and health related quality of life. Immunology outcomes were excluded. Only studies reported in English were included in the review.

The dose of fingolimod was not specified in the inclusion criteria. However, the submission identified but subsequently excluded from consideration one RCT, and its extension studies, which assessed fingolimod at doses of 1.25 and 5.00 mg/day, above the licensed indication of 0.5 mg/day. Whilst the relevant dose would ideally have been stated in the inclusion criteria, the criteria appeared appropriate to ensure the identification of relevant trials of fingolimod and appropriate comparators in the population defined in the NICE scope. The NICE scope is broader than the populations defined in the Committee for Medicinal Products for Human Use (CHMP) approval and the adoption of the wider criterion of RRMS was appropriate to capture all relevant studies.

Economic Evaluation

ERG Comment and Critique on Manufacturer's Review of Cost-effectiveness Evidence

The manufacturer's review was primarily aimed at the identification of previously published cost-effectiveness studies of fingolimod for the treatment of adults with RRMS. Additional aims included the identification of reviews of utility estimates in multiple sclerosis and reviews of resource use and cost estimates in multiple sclerosis. The databases searched for the cost-effectiveness section included all of those specified by NICE in the specification for manufacturer/sponsor submission of evidence; MEDLINE, MEDLINE In-Process, EMBASE, EconLIT and NHS EED. Searches were also carried out of the Cochrane Library, including:

- The Cochrane Database of Systematic Reviews
- The Cochrane Central Register of Controlled Trials
- The Database of Abstracts of Reviews of Effects
- The Health Technologies Assessment database

A group of organisation's websites were also searched to identify conference abstracts and unpublished studies; these were:

- The International Society for Pharmacoeconomics and Outcomes Research
- The American Academy of Neurology
- The Americas Committee for Treatment and Research in Multiple Sclerosis
- The European Committee for Treatment and Research in Multiple Sclerosis
- The European Charcot Foundation

In addition the NICE website was searched to identify any relevant Health Technology Assessment reports as well as a search of the bibliographies of the 'seminal' papers.

The submission gave detailed descriptions of the search strategies used to obtain papers from the databases and met NICE requirements. It included the specific databases searched; the service providers used; the dates when searches were conducted; the date spans of the searches; and the complete strategies used. The strategies aimed to retrieve all research relating to multiple sclerosis, treatments for multiple sclerosis, utility studies and economic evaluation. The terms used for each search facet were appropriate. Truncation and wildcards were used appropriately.

The ERG considers the search strategy for cost-effectiveness to be appropriate. The ERG believes that the searches were unlikely to miss any published studies relating to any of the three aims of the search strategy that could be potentially useful in the cost-effectiveness section of the submission.

No references that met the primary aim of the search were found.

Number of Source Documents

Clinical Effectiveness

- Two randomised controlled trials (RCTs) were included for direct treatment comparison.
- Sixteen additional studies were included for mixed treatment comparison (MTC).

Cost-effectiveness

- No published cost-effectiveness analyses were identified.
- The manufacturer submitted an economic model

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Evidence Review Group (ERG) report for this appraisal was prepared by the Centre for Review and Dissemination (CRD) and Centre for Health Economics (CHE) Technology Assessment Group (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description and Critique of Manufacturers Approach to Validity Assessment

The ERG's validity assessment of the two studies (TRANSFORMS and FREEDOMS) used by the manufacturer for direct comparisons is shown in Table 3 of the ERG report (see the "Availability of Companion Documents" field).

The studies included in the mixed treatment comparison (MTC) were appraised (in manufacturer's submission) using the criteria of randomisation methods and blinding. Whilst these deal with some basic aspects of trial validity they do not consider allocation concealment, use of an intention-to-treat analysis, selective outcome reporting or the use of a power calculation. The results of the appraisal indicated that most trials were of reasonable quality, based on the criteria assessed.

The ERG did not replicate the validity assessment of the trials in the MTC; since the MTC is not used to inform the economic model this was not considered necessary.

Describe and Critique the Statistical Approach Used

The two trials of head-to head comparisons (TRANSFORMS and FREEDOMS) appraised fingolimod 0.5 mg and 1.25 mg compared, respectively to Avonex 30 µg and to placebo. Consequently there was no attempt statistically to combine the efficacy data from these trials in the clinical effectiveness sections of the submission; this was clearly appropriate.

The fingolimod 0.5 mg arms were combined in the analysis of safety outcomes for comparison with data from the Avonex arm of the TRANSFORMS trial and the placebo arm of the FREEDOMS trial respectively. This appeared reasonable despite the differences between the trials.

Whilst the head-to-head comparisons reported hazard ratios (HRs) for efficacy outcomes, the MTC employed relative risks (RRs). This is potentially problematic as, unlike an odds ratio, the RR is not symmetric. This fact has been demonstrated to be capable of generating anomalous results in an indirect comparison, including for an analysis comparing natalizumab with interferon therapy for the outcome of progression. A further point to note is that the MTC was conducted using PROC GLIMMIX in SAS; this is known to incorporate lower levels of uncertainty around the means than WINBUGS. Therefore it is possible that the analysis may not reflect the full extent of the heterogeneity which was apparent between the trials.

Critique of Submitted Evidence Syntheses

The only synthesis of the two head-to-head trials consisted of a pooling of the fingolimod 0.5 mg arms for the assessment of adverse events relative to the placebo arm of FREEDOMS and the Avonex arm of TRANSFORMS.

An MTC of 18 trials attempted to provide evidence of fingolimod's efficacy on key outcomes of annualised relapse rate (ARR), disability progression and treatment discontinuation due to adverse events. These included trials that had populations who met criteria for relapsing–remitting multiple sclerosis (RRMS) but not necessarily for any of the populations defined by Committee for Medicinal Products for Human Use (CHMP). The submission did not attempt the post-hoc identification of subgroups within these trials. There was also, as the submission noted, very considerable clinical heterogeneity between the trials with respect to permitted and actual prior use of disease-modifying therapy (DMT), duration, and criteria used to define disability progression. An exploration of covariates did not indicate any variables with consistent statistically significant effects on all treatment endpoints. However, two covariates with statistical significance were identified for each of ARR and disability progression.

As a consequence of the heterogeneity, and the fact that it was based on general RRMS populations, the MTC was not subsequently used to inform the economic model.

See Section 4 of the ERG report (see the "Availability of Companion Documents" field) for more information.

Economic Evaluation

The cost-effectiveness evaluation used a decision model, designed as a Markov model, to model disease progression using 21 health states representing different degrees of disease severity and death. Disability progression and conversion to secondary progressive multiple sclerosis (SPMS) were assumed irreversible. The model also accounted for relapses, adverse events, withdrawal and death. Although the occurrence of relapses did not influence the way in which progression was modelled to occur, relapse was modelled to depend on expanded disability status scale (EDSS) score. After withdrawing from fingolimod or Avonex patients were assumed to receive best supportive care (BSC).

The perspective of the analysis of costs was that of the National Health Service (NHS) and Personal Social Services (PSS). Costs were separated into disease costs, administration and monitoring costs and drug acquisition costs. Quality-adjusted life years (QALYs) were used as the measure of outcomes. Both patient and caregiver utility were accounted for and varied by disease severity. Utility adjustments were also applied to account for relapses and adverse events. Treatment with fingolimod or Avonex was assumed to be provided only to RRMS patients with an EDSS score of between 0.0 and 6.0. Patients were modelled to continue to receive these treatments until the treatment was either withdrawn (due to adverse events, disease progression to an EDSS score of above 6 or conversion to SPMS) or a patient died. A 50 year time horizon was used in the model to 'sufficiently capture differences in costs and outcomes'; previous appraisals in MS assessed by NICE adopted time-horizons lower than or equal to 20 years (TA 32 and TA 127). Both costs and benefits were discounted at 3.5%.

Both deterministic and probabilistic sensitivity analysis were carried out by the manufacturer to demonstrate the level of uncertainty around the model results. Despite the non-linear nature of the model, only the deterministic results were presented in the manufacturer's submission.

Summary and Critique of Manufacturer's Submitted Economic Evaluation by the ERG

An overall summary of the manufacturer's approach and signposts to the relevant sections in the manufacturer's submission are reported in Table 7 of the ERG report (see the "Availability of Companion Documents" field).

Table 8 of the ERG report summarises the economic submission using a checklist based on NICE's reference case and other methodological recommendations, and the ERG's comments on whether the de-novo evaluation meets the requirements of these recommendations.

Model Validation

Model validation was dealt with by the manufacturer in a limited manner and seems to have been restricted to checking that formulas in spreadsheets were typed correctly and ensuring referenced values were copied into the model correctly. Some extreme value testing of the model was carried out to ensure that the model behaved as it was described to in the submission (e.g., setting mortality rate to 0 and observing that the model predicts no deaths).

No internal validation or goodness of fit was reported comparing the model predictions with observations from the FREEDOMS, TRANSFORMS or Ontario studies, the three main sources of evidence used to inform the model. No external validation was reported comparing the model predicted results with other trials or other published model results. Clinical expertise was not utilised to verify that the model captured a plausible abstraction of the disease or made clinically plausible predictions.

The ERG has attempted to check the model predictions against the results observed in the trials throughout the current section and have consistently found divergences between them.

See Sections 5 and 6 of the ERG report (see the "Availability of Companion Documents" field) for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The manufacturer submitted a de novo economic model that is structurally similar to models used in previous National Institute for Health and Clinical Excellence (NICE) technology appraisal guidance on treatments for multiple sclerosis. The model is based on a Markov cohort approach and estimates disease progression through 21 disability states that are defined by Expanded Disability Status Scale (EDSS) score (ranging from 0 to 10) and account for disability for patients with relapsing–remitting multiple sclerosis (10 states), patients with secondary progressive multiple sclerosis (10 states) and death.

The original base-case incremental cost-effectiveness ratio (ICER) for fingolimod compared with Avonex was £55,634 per quality-adjusted life year (QALY) gained for population 1b (consisting of people with highly active relapsing–remitting multiple sclerosis with at least one relapse in the previous year while on treatment with beta interferon and at least nine T2-hyperintense lesions on a brain MRI or at least one gadolinium-enhancing lesion; patient access scheme not included). Cost-effectiveness analyses for population 1a and population 2 (defined in section 3.1 of the original guideline document) were not provided by the manufacturer. One-way sensitivity analyses suggested that the ICER for fingolimod compared with Avonex was most sensitive to the relative risks of disease progression assumed for fingolimod and Avonex, and the relative risk of relapse for Avonex. Uncertainty in all other parameter values led to only small changes in the ICER. Results of a probabilistic sensitivity analysis showed that there was a 12% probability that the base-case ICER was less than £20,000 per QALY gained, and a 26% probability that it was less than £30,000 per QALY gained.

The Evidence Review Group (ERG) was concerned about the resources and costs assumed in the manufacturer's original model. The ERG was

unclear why the costs associated with only some severe adverse reactions were included in the model, and why the costs associated with non-serious adverse reactions were not included. The ERG was also unclear whether costs associated with relapsing–remitting multiple sclerosis were different from those associated with secondary progressive multiple sclerosis.

The ERG noted that although the manufacturer had included a probabilistic model in its original submission, the cost-effectiveness results presented in the original submission were deterministic. The ERG provided a probabilistic analysis for the manufacturer's original base case that gave an ICER of £69,787 per QALY gained for fingolimod compared with Avonex (patient access scheme not included). This ICER was noted to be substantively higher than the manufacturer's original deterministic estimate of £55,634 per QALY gained.

The ERG was concerned about the representativeness of the initial EDSS score distribution used in the manufacturer's original model. The ERG examined a number of scenarios and showed that the cost-effectiveness of fingolimod varies depending on the initial distribution of patients across EDSS states.

The ERG noted that the baseline relapse rates in the manufacturer's original model were dependent on EDSS state but were then adjusted by the relative risk of relapse with a particular disease-modifying therapy compared with best supportive care. The ERG was concerned that these estimates for relative effect were taken from different data sets and therefore had no implicit correlation. In addition, the ERG cautioned that the impact of disease-modifying therapy could be double-counted in the model.

Summary of Appraisal Committee's Key Conclusions

The Committee noted the concerns of the clinical specialists that the model may not reflect the natural history of multiple sclerosis, because it does not allow for improvement in EDSS scores. The Committee concluded that the manufacturer's approach was reasonable because few people experience an improvement in EDSS score in clinical practice.

The Committee noted potential inaccuracies in some of the administration costs included in the manufacturer's original model. The Committee noted that the manufacturer had corrected these inaccuracies in the revised analyses submitted in response to the appraisal consultation documents and was persuaded that revising the costs in the model had a minimal impact on the ICER.

The Committee acknowledged that there was variation in current practice and therefore concluded that fingolimod should be compared with a weighted average of the comparators currently used in UK clinical practice to manage relapsing–remitting multiple sclerosis. This includes best supportive care together with a mix of beta interferons (with the proportions for the beta interferons based on market share data from the Prescription Pricing Authority).

The Committee concluded that depending on the proportions assumed for the comparator treatments, and the assumptions included in the model about the natural history of disability progression and the waning of treatment effect after 5 years, the most plausible ICER for fingolimod compared with the weighted average of the comparators from the manufacturer's model was likely to be in the range of £25,000 to £35,000 per QALY gained. The Committee recognised that including all of the benefits of fingolimod which may not be adequately captured in the QALY calculation (as suggested by the manufacturer and the patient experts) could decrease the ICER to a level that would be considered a cost-effective use of National Health Service (NHS) resources.

See Sections 3 and 4 of the original guideline document for details of the economic analyses provided by the manufacturers, the ERG comments, and the Appraisal Committee considerations.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups

were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of fingolimod and a review of this submission by the Evidence Review Group (ERG). For clinical effectiveness, two randomised controlled trials (RCTs) were the main source of evidence. For cost-effectiveness, the manufacturer's economic model was considered.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of fingolimod for the treatment of highly active relapsing–remitting multiple sclerosis

Potential Harms

The most common adverse reactions to treatment with fingolimod include influenza virus infections, headaches, diarrhoea and elevated liver enzyme activity. The summary of product characteristics (SPC) states that 'macular oedema with or without visual symptoms has been reported in 0.4% of patients treated with fingolimod 0.5 mg, occurring predominantly in the first 3–4 months of therapy. An ophthalmological evaluation is therefore recommended at 3–4 months after treatment initiation'.

For full details of adverse reactions and contraindications, see the SPC.

Contraindications

Contraindications

For full details of adverse reactions and contraindications, see the summary of product characteristics (SPC).

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute of Clinical Health and Excellence (NICE), and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- The Secretary of State and the Welsh Assembly Minister for Health and Social Services have issued directions to the National Health Service (NHS) in England and Wales on implementing National Institute for Health and Clinical Excellence (NICE) technology appraisal guidance. When a NICE technology appraisal recommends use of a drug or treatment, or other technology, the NHS must usually provide funding and resources for it within 3 months of the guidance being published. If the Department of Health issues a variation to the 3-month funding direction, details will be available on the NICE website. When there is no NICE technology appraisal guidance on a drug, treatment or other technology, decisions on funding should be made locally.
- NICE has developed tools to help organisations put this guidance into practice (listed below).
  - Costing template and report to estimate the national and local savings and costs associated with implementation
  - Audit support for monitoring local practice
- The Department of Health and the manufacturer have agreed that fingolimod will be offered to the NHS under a patient access scheme which makes fingolimod available with a discount on the list price. The size of the discount is commercial in confidence. It is the responsibility of the manufacturer to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to Novartis Pharmaceuticals UK's commercial operations team on 01276 698717 or Commercial.Team@novartis.com.

Implementation Tools

Audit Criteria/Indicators

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Apr. 55 p. (Technology appraisal guidance; no. 254).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Apr

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Dr Amanda Adler (*Chair*), Consultant Physician, Addenbrooke's Hospital, Cambridge; Professor Ken Stein (*Vice Chair*), Professor of Public Health, Peninsula Technology Assessment Group (PenTAG), University of Exeter; Professor Keith Abrams, Professor of Medical Statistics, University of Leicester; Dr Ray Armstrong Consultant Rheumatologist, Southampton General Hospital; Dr Jeff Aronson, Reader in Clinical Pharmacology, University Department of Primary Health Care, University of Oxford; Dr Peter Barry, Consultant in Paediatric Intensive Care, Leicester Royal Infirmary; Dr Michael Boscoe, Consultant Cardiothoracic Anaesthetist, Royal Brompton and Harefield NHS Foundation Trust; Professor John Cairns, Professor of Health Economics Public Health and Policy, London School of Hygiene and Tropical Medicine; Dr Mark Chakravarty, External Relations Director – Pharmaceuticals & Personal Health, Oral Care Europe; Mark Chapman, Health Economics and Market Access Manager, Medtronic UK; Professor Fergus Gleeson, Consultant Radiologist, Churchill Hospital, Oxford; Eleanor Grey, Lay member; Sanjay Gupta, Young physically disabled (YPD) Service Case Manager, Southwark Health and Social Care, Southwark Primary Care Trust; Dr Neil Iosson, General Practitioner; Terence Lewis, Lay member; Professor Ruairidh Milne, Director of Strategy and Development and Director for Public Health Research at the National Institute for Health Research (NIHR) Evaluation, Trials and Studies Coordinating Centre at the University of Southampton; Dr Peter Norrie, Principal Lecturer in Nursing, DeMontfort University, Leicester; Dr Sanjeev Patel, Consultant Physician and Senior Lecturer in Rheumatology, St Helier University Hospital, Carshalton; Dr John Pounsford, Consultant Physician, Frenchay Hospital, Bristol; Dr Casey Quinn, Lecturer in Health Economics, Division of Primary Care, University of Nottingham; Alun Roebuck, Consultant Nurse in Critical and Acute Care, United Lincolnshire NHS Trust; Dr Florian Alexander Ruths, Consultant, Psychiatrist and Cognitive Therapist at the Maudsley Hospital, London; Navin Sewak, Primary Care Pharmacist, NHS Hammersmith and Fulham; Roderick Smith, Finance Director, West Kent Primary Care Trust; Cliff Snelling, Lay member; Professor Andrew Stevens, Professor of Public Health, Department of Public Health and Epidemiology, University of Birmingham; Professor Rod Taylor, Professor in Health Services Research, Peninsula Medical School, Universities of Exeter and Plymouth; Dr Colin Watts, Consultant Neurosurgeon, Addenbrooke's Hospital, Cambridge; Tom Wilson, Director of Contracting & Performance, NHS Tameside & Glossop

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis. Costing template. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012. (Technology appraisal guidance; no. 254). Electronic copies: Available from the National Institute for Health and Clinical Excellence (NICE) Web site .
- Fingolimod for highly active relapsing–remitting multiple sclerosis. Clinical audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012. (Technology appraisal guidance; no. 254). Electronic copies: Available from the NICE Web site .
- Fingolimod for highly active relapsing–remitting multiple sclerosis. Electronic audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012. (Technology appraisal guidance; no. 254). Electronic copies: Available from the NICE Web site .
- Fingolimod for the treatment of relapsing remitting multiple sclerosis. Evidence Review Group report. York (UK): Centre for Reviews and Dissemination, University of York; 2011. 128 p. Electronic copies: Available in PDF from the NICE Web site .

Patient Resources

The following is available:

- Fingolimod for highly active relapsing–remitting multiple sclerosis. Understanding NICE guidance. Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Apr. 6 p. (Technology appraisal guidance; no. 254). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on July 18, 2012. This summary was updated by ECRI Institute on August 11, 2015 following the U.S. Food and Drug Administration advisory on Gilenya (fingolimod).

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their Technology Appraisal guidance with the intention of disseminating and facilitating the implementation of that guidance. NICE has not verified this content to confirm that it accurately reflects the original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE technology appraisal guidance is prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk .

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